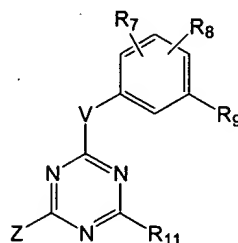


**IN THE CLAIMS:**

Below is a complete listing of all claims (following entry of the amendment of July 30, 2003), and replaces all prior versions.

1-65. (Canceled).

66 (Currently amended). A compound of Formula (I),



**I**

or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from  $-\text{CHR}^5-$ ,  $-\text{NR}^5-$ ,  $-\text{O}-$ , and  $-\text{S}-$ ;

Z is chosen from halogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl,  $-\text{SR}^3$ ,  $-\text{OR}^3$ , and  $-\text{N}(\text{R}^1)(\text{R}^2)$ ;  $-\text{N}(\text{R}^1)(\text{R}^2)$  taken together may form a heterocyclyl or substituted heterocyclyl; or

R<sup>1</sup> is chosen from hydrogen, alkyl and substituted alkyl; and

R<sup>2</sup> is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R<sup>3</sup> is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R<sup>5</sup> is chosen from hydrogen and alkyl, or when attached to a nitrogen atom, R<sup>5</sup> taken together with R<sup>7</sup> may form a fused heterocyclyl or substituted heterocyclyl;

R<sup>7</sup> is chosen from hydrogen,  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ , halogen, cyano, alkyl, substituted alkyl, alkoxy, and alkylthio, or when V is  $-\text{NR}^5$ ,  $-\text{R}^5$  and R<sup>7</sup> taken together may form a fused heterocyclyl or substituted heterocyclyl;

R<sup>8</sup> is chosen from hydrogen and halogen;

$R^9$  is chosen from  $-\text{CO}_2(\text{alkyl})$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{SO}_2\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{SO}_2\text{R}^{34}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ ,  $-\text{CH}_2\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ ,  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{CH}_2\text{OC}(\text{O})\text{R}^{34}$ ,  $\text{C}_{1-6}\text{alkyl}$ , substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, and  $-\text{C}(\text{O})\text{R}^{10}$ ; provided, however, that when  $R^9$  is  $\text{CH}_3$  or  $\text{NH}_2$ , then neither  $R^2$  nor  $R^{14}$  is *para*-cyano-phenyl;

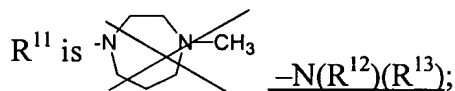
or  $R^8$  and  $R^9$  taken together may form  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{CH}_2-$  or  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{C}(\text{O})-$ ;

$R^{10}$  is chosen from heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkyl, and substituted alkyl;

$R^{31}$  and  $R^{33}$  are independently chosen from hydrogen, alkyl, and substituted alkyl;

$R^{32}$  is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

$R^{34}$  is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;



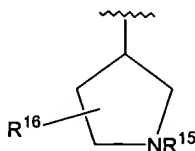
$R^{12}$  is chosen from hydrogen, alkyl, and substituted alkyl; and

$R^{13}$  is  $-(\text{CH}_2)_m\text{R}^{14}$ ; or

$-\text{N}(\text{R}^{12})(\text{R}^{13})$  taken together may form a heterocyclyl or substituted heterocyclyl;

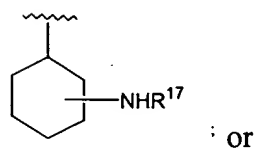
$m$  is 0, 1, 2 or 3;

$R^{14}$  is chosen from ~~hydrogen~~, alkyl, substituted alkyl,  $-\text{C}(\text{O})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ , aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, and



$R^{15}$  is chosen from hydrogen, alkyl, substituted alkyl, alkenyl,  $-\text{C}(\text{O})$ -alkyl,  $-\text{C}(\text{O})$ -substituted alkyl,  $-\text{C}(\text{O})$ -aryl,  $-\text{C}(\text{O})$ -substituted aryl,  $-\text{C}(\text{O})$ -alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

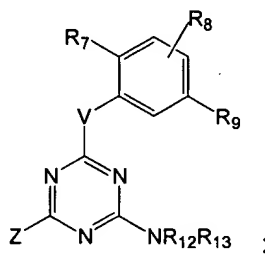
$R^{16}$  is chosen hydrogen, alkyl, substituted alkyl, and



$R^{17}$  is chosen from hydrogen, alkyl, substituted alkyl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, and -C(O)-substituted aryl.

67-69 (Canceled).

70. (Currently amended). A compound having the formula,



or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from  $-\text{CHR}^5$ -,  $-\text{NR}^5$ -,  $-\text{O}$ -, and  $-\text{S}$ -;

Z is halogen, alkyl,  $-\text{N}(\text{R}^1)(\text{R}^2)$ , or alkyl substituted with one to two of  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ , alkoxy, alkylthio, halogen, cyano, carboxyl, hydroxyl,  $-\text{SO}_2$ -alkyl,  $-\text{CO}_2$ -alkyl, -C(O)-alkyl, nitro, cycloalkyl, substituted cycloalkyl,  $-\text{C}(\text{O})-\text{N}(\text{R}^{31})(\text{R}^{32})$ , and/or  $-\text{NH}-\text{C}(\text{O})$ -alkyl;

$\text{R}^1$  is hydrogen or methyl;

$\text{R}^2$  is alkyl of 1 to 8 carbon atoms;

$\text{R}^3$  is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$\text{R}^5$  is chosen from hydrogen and alkyl of 1 to 4 carbon atoms;

$\text{R}^7$  is chosen from hydrogen, amino, amino $\text{C}_{1-4}$ alkyl, halogen, cyano,  $\text{C}_{1-4}$ alkyl,  $\text{C}_{1-4}$ alkoxy, and alkylthio;

$\text{R}^8$  is attached to any available carbon atom of the phenyl ring and is chosen from hydrogen and halogen;

$R^9$  is chosen from  $-C(O)N(R^{31})(R^{32})$ ,  $-SO_2N(R^{31})(R^{32})$ ,  
 $-N(R^{33})SO_2R^{34}$ ,  $-C(O)N(R^{33})N(R^{31})(R^{32})$ ,  $-N(R^{33})C(O)R^{34}$ ,  $-CH_2N(R^{33})C(O)R^{34}$ ,  
 $-N(R^{31})(R^{32})$ ,  $-CH_2OC(O)R^{34}$ , heterocyclyl, and substituted heterocyclyl; or

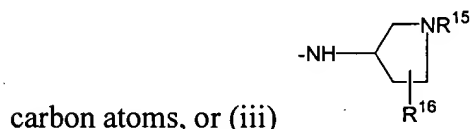
$R^8$  and  $R^9$  taken together may form  $-C(O)N(R^{33})CH_2-$  or  $-C(O)N(R^{33})C(O)-$ ;

$R^{31}$  and  $R^{33}$  are independently chosen from hydrogen, alkyl, and substituted alkyl;

$R^{32}$  is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl,  
cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

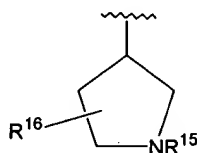
$R^{34}$  is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted  
cycloalkyl, heterocyclyl and substituted heterocyclyl;

$-N(R^{12})(R^{13})$  taken together form (i) a monocyclic heterocyclyl or substituted heterocyclyl of  
5 to 7 atoms having 1, 2 or 3 additional nitrogen atoms, (ii)  $-NH$ -alkyl wherein alkyl is of 1 to 4



~~$m$  is 0, 1, 2 or 3;~~

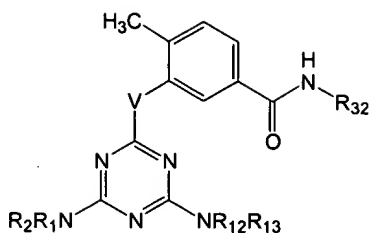
~~$R^{14}$  is chosen from hydrogen, alkyl, substituted alkyl,  $-C(O)N(R^{21})(R^{22})$ ,  
 $-N(R^{23})C(O)R^{24}$ , aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted  
heterocyclyl and~~



$R^{15}$  and  $R^{16}$  are independently hydrogen or methyl; and

$R^{17}$  is chosen from hydrogen, alkyl, substituted alkyl,  $-C(O)$ -alkyl,  
 $-C(O)$ -substituted alkyl,  $-C(O)$ -aryl, and  $-C(O)$ -substituted aryl.

71 (Previously presented ). A compound of Claim 70 or a enantiomer, diastereomer,  
tautomer, or pharmaceutically-acceptable salt, or solvate thereof, having the formula:



72 (Currently amended). The compound of claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

$R^7$  is halogen, methyl, methoxy, halogen, or cyano.

73 (Currently Amended ). The compound of claim 70 or an ~~stereoisomer~~ enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, ~~prodrug~~, or solvate thereof, wherein:

$R^9$  is  $C(=O)NH_2$ ,  $C(=O)NH(CH_3)$ , or  $C(=O)NHO(CH_3)$ .

74 (Currently Amended ). The compound of claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof,

wherein  $R^7$  is methyl and  $R^9$  is  $C(=O)NH(CH_3)$  or  $C(=O)NHO(CH_3)$ .

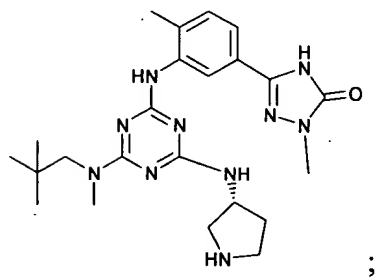
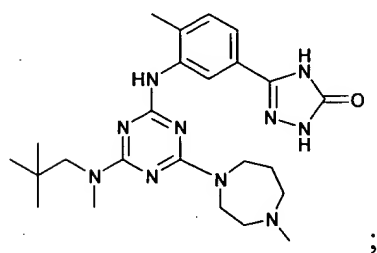
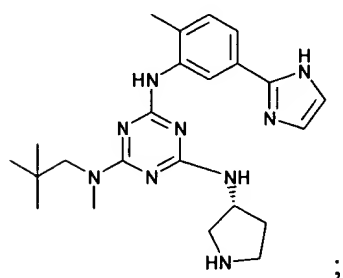
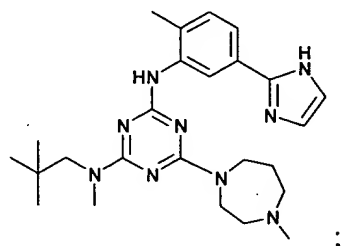
75 (Currently Amended ). A compound of Claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof wherein:

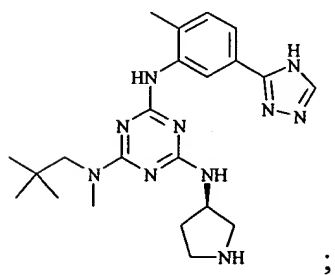
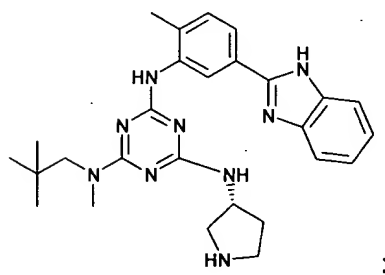
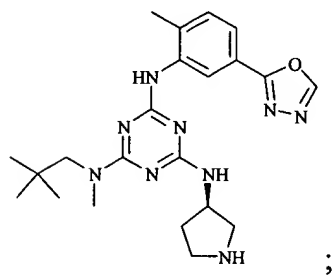
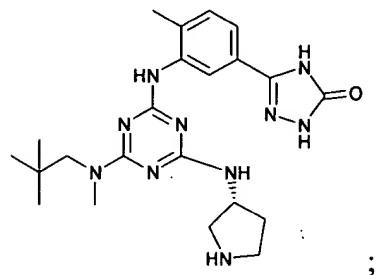
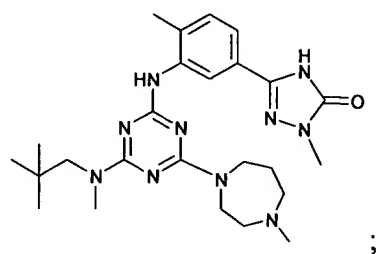
$R^9$  is chosen from unsubstituted or substituted triazolyl, oxadiazolyl, imidazolyl, thiazolyl and benzimidazolyl.

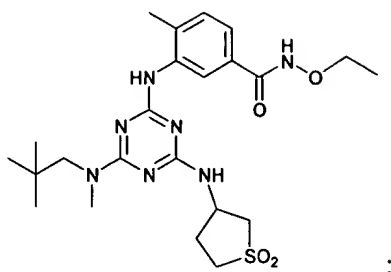
76 (Currently Amended ). A compound of Claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof wherein:

$R^9$  is chosen from substituted or unsubstituted 1,2,4-triazole; substituted or unsubstituted thiazole connected via a C2, C4, or C5 position; substituted or unsubstituted 1,3,4-oxdiazole connected via a 2 or 5 position; and substituted or unsubstituted imidazole connected via a C2, C4, C5, N1 or N3 position.

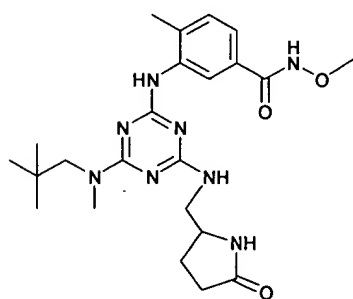
77 (Currently Amended ). A compound which is selected from (i):



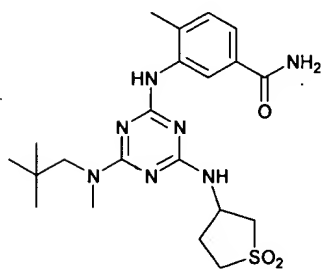




;



; and



; or (ii) an enantiomer, diastereomer, tautomer, or

pharmaceutically-acceptable salt, or solvate of the compound selected from paragraph (i).

78 (Currently Amended ). A pharmaceutical composition comprising as an active ingredient, a compound, or a ~~prodrug or~~ salt thereof, according to claim 70, and a pharmaceutically acceptable carrier.



79 (Previously presented). A pharmaceutical composition according to claim 78, further comprising one or more additional active ingredients.

80 (Previously presented). A pharmaceutical composition according to claim 79, wherein said additional active ingredient is an anti-inflammatory compound or an immunosuppressive agent.

81 (Previously presented). A pharmaceutical composition according to claim 79, wherein said additional active ingredient is chosen from a steroid and an NSAID.

82 (Currently Amended). A method of treating rheumatoid arthritis, the method comprising administering to a mammal ~~in need of such treatment~~, an effective amount of a composition according to claim 78.

83-84 (Canceled).

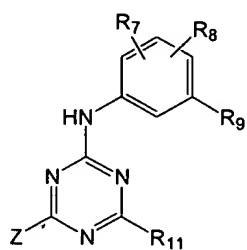
85 (Previously presented). The method according to claim 82 wherein said composition according to claim 78 is administered with one or more additional anti-inflammatory or immunosuppressive agents as a single dose form or as separate dosage forms.

86-87 (Canceled).

88 (Previously presented). A method of inhibiting TNF- $\alpha$  expression in a mammal, the method comprising administering to the mammal an effective amount of a composition according to Claim 78.

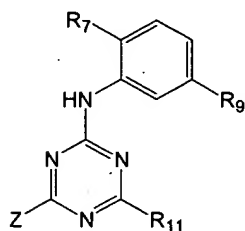
89-95 (Canceled).

96 (New). A compound according to claim 66, having the formula,



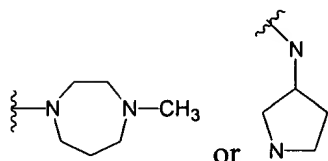
, or pharmaceutically-acceptable salt or solvate thereof.

97 (New). A compound according to claim 66, having the formula,



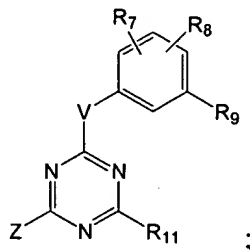
or pharmaceutically-acceptable salt or solvate thereof.

98 (New). A compound according to claim 66, wherein R<sub>11</sub> is



or pharmaceutically-acceptable salt or solvate thereof.

99 (New). A method of modulating p38 kinase in a mammal comprising administering to the mammal at least one compound having the formula,



or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from  $-\text{CHR}^5$ -,  $-\text{NR}^5$ -,  $-\text{O}$ -, and  $-\text{S}$ -;

Z is chosen from halogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl,  $-\text{SR}^3$ ,  $-\text{OR}^3$ , and  $-\text{N}(\text{R}^1)(\text{R}^2)$ ;  $-\text{N}(\text{R}^1)(\text{R}^2)$  taken together may form a heterocyclyl or substituted heterocyclyl; or

$\text{R}^1$  is chosen from hydrogen, alkyl and substituted alkyl; and

$\text{R}^2$  is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$\text{R}^3$  is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$\text{R}^5$  is chosen from hydrogen and alkyl, or when attached to a nitrogen atom,  $\text{R}^5$  taken together with  $\text{R}^7$  may form a fused heterocyclyl or substituted heterocyclyl;

$\text{R}^7$  is chosen from hydrogen,  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ , halogen, cyano, alkyl, substituted alkyl, alkoxy, and alkylthio, or when V is  $-\text{NR}^5$ ,  $-\text{R}^5$  and  $\text{R}^7$  taken together may form a fused heterocyclyl or substituted heterocyclyl;

$\text{R}^8$  is chosen from hydrogen and halogen;

$\text{R}^9$  is chosen from  $-\text{CO}_2(\text{alkyl})$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{SO}_2\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{SO}_2\text{R}^{34}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ ,  $-\text{CH}_2\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ ,  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{CH}_2\text{OC}(\text{O})\text{R}^{34}$ ,  $\text{C}_{1-6}\text{alkyl}$ , substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, and  $-\text{C}(\text{O})\text{R}^{10}$ ; provided, however, that when  $\text{R}^9$  is  $\text{CH}_3$  or  $\text{NH}_2$ , then neither  $\text{R}^2$  nor  $\text{R}^{14}$  is *para*-cyano-phenyl;

or  $\text{R}^8$  and  $\text{R}^9$  taken together may form  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{CH}_2$ - or  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{C}(\text{O})$ -;

$\text{R}^{10}$  is chosen from heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkyl, and substituted alkyl;

$\text{R}^{31}$  and  $\text{R}^{33}$  are independently chosen from hydrogen, alkyl, and substituted alkyl;

$\text{R}^{32}$  is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

$\text{R}^{34}$  is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$\text{R}^{11}$  is  $-\text{N}(\text{R}^{12})(\text{R}^{13})$ ;

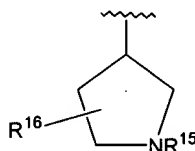
$\text{R}^{12}$  is chosen from hydrogen, alkyl, and substituted alkyl;

$R^{13}$  is  $-(CH_2)_mR^{14}$ ;

$-N(R^{12})(R^{13})$  taken together may form a heterocyclyl or substituted heterocyclyl;

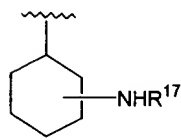
$m$  is 0, 1, 2 or 3;

$R^{14}$  is chosen from hydrogen, alkyl, substituted alkyl,  $-C(O)N(R^{31})(R^{32})$ ,  $-N(R^{33})C(O)R^{34}$ , aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, and



$R^{15}$  is chosen from hydrogen, alkyl, substituted alkyl, alkenyl,  $-C(O)$ -alkyl,  $-C(O)$ -substituted alkyl,  $-C(O)$ -aryl,  $-C(O)$ -substituted aryl,  $-C(O)$ -alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$R^{16}$  is chosen hydrogen, alkyl, substituted alkyl, and



or

$R^{17}$  is chosen from hydrogen, alkyl, substituted alkyl,  $-C(O)$ -alkyl,  $-C(O)$ -substituted alkyl,  $-C(O)$ -aryl, and  $-C(O)$ -substituted aryl.